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# SUCROSE ACETATE ISOBUTYRATE BASED NANOGELS AS LIQUID FIDUCIAL TISSUE MARKERS WITH POTENTIAL USE IN IMAGE GUIDED RADIOTHERAPY

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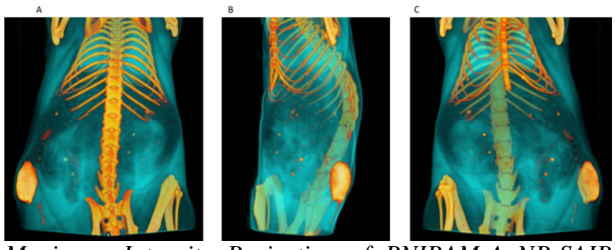
## SUMMARY
**S**ucrose **A**cetate **I**so**B**utyrate (SAIB)-based radiopaque fiducial tissue markers containing coated gold nanoparticles (AuNPs) have been developed. One of these formulations, the PNIPAM (poly(N-isopropyl acrylamide))-AuNP-SAIB based gel, was assessed to be a suitable marker for image guided radiotherapy (IGRT).

## INTRODUCTION
IGRT is an important tool used to visualize tumors during radiation treatment. Tumors rarely display a fixed position during irradiation or within a treatment period due to breathing motion, changes in organ filling and tumor size. Radiopaque fiducial tissue markers are therefore of great interest to place within - or around tumors in order to achieve high precision in IGRT. Better markers will enable improved tumor coverage i.e. the destruction of all cancer tissue. Furthermore, it is important to have a safer and more accurate setup for tumor treatment in radiotherapy - including adaptation of online "tumor-tracking" – thereby delivering high radiation doses to tumors with minimal damage to surrounding healthy tissue **[1]**.

## EXPERIMENTAL METHODS
The poster presents the development of novel injectable liquid fiducial markers based on formulations of SAIB and polylactide (PLA) containing coated AuNPs. A mixture of SAIB/EtOH/PLA (75:20:5) was used as matrix due to its high biocompatibility, low viscosity, as well as its ability to form a stable, biodegradable gel depot upon injection **[2]**. Three different AuNP coating systems were tested – a dithiolane functionalized SAIB derivative, synthesized in four steps starting from sucrose, together with PEG- and PNIPAM polymers, respectively. The AuNPs were synthesized by a three step seeding protocol using chloroauric acid as $Au^{3+}$ source and trisodium citrate as reductant and stabilizer. *In vitro* release from SAIB gels was studied in PBS-buffer at $37^0$C. Gels (200µL) containing SAIB/EtOH/PLA (75:20:5) + 30mg PNIPAM-AuNPs $mL^{-1}$ or 10mg PEG-AuNPs $mL^{-1}$ were injected subcutaneously at the upper left flank of immunocompetent NMRI-mice using hypodermic 25G needles. The gel-depots were visualized by micro-CT imaging.

## RESULTS AND DISCUSSION
The dithiolane functionalized SAIB derivative was discarded as a coating option due to irreversible aggregation of the formed nanoparticles. The SAIB gels containing PEGylated AuNPs provided high CT contrast *in vivo*, however it suffered from AuNP migration towards the gel-boundaries resulting in an inhomogeneous distribution of contrast agent. The PNIPAM-coated-AuNP-SAIB gel provided both excellent CT contrast and high *in vivo* stability. Furthermore, the PNIPAM-coated-AuNPs are easy to handle, as they can be lyophilized and stored as an air stable powder, which is readily dispersible in ethanol.



*Maximum Intensity Projection of PNIPAM-AuNP-SAIB gel depot in a mouse viewed from several angles.*

## CONCLUSION
The PNIPAM-AuNP-SAIB gel showed high stability, biocompatibility and provided high CT contrast *in vivo*. This gel is a viable alternative to existing liquid fiducial markers.

## REFERENCES
1. Engstrom P.E., Haraldsson P., Landberg T., et al., *Acta Oncol.* ***44(6)***, 572-578 (2005)
2. Jølck, R. I., Binderup T, Hansen A.E., et al. *Adv. Healthcare Mater.* (2014).